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RESULTS OF RADIATION THERAPY OF EARLY CARCINOMA OF THE VOCAL CORDS

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Carcinoma of the larynx is common among males in some parts of Latin America, France, North Africa, the Eastern Mediterranean and India. The age-standardized mortality rates per 100 000 males of laryngeal carcinoma are 19.6 in Brazil, 11.4 in Argentina and 11.1 in France, but in Japan the rate is 1.8 only (DUNHAM & BAILOR 1968). It is one of the characteristics in Japan that the incidence of supraglottic tumors is higher than glottic ones (IWAMOTO 1971). The districts with high ratios of carcinoma of the larynx are located in West Japan, particularly in Kinki District (SEGI et coll. 1965). Approximately 700 patients with laryngeal carcinoma have been annually registered by Head and Neck Society of Japan (IWAMOTO 1971). At Osaka University Hospital, located in Kinki District, about 100 patients are annually registered; glottic tumors have increased steadily in number, now being 50 per cent of all laryngeal carcinomas. At the same time the average age of the patients has become higher. SMITH et coll. (1973) reported that patients with glottic tumors were slightly older than those with supraglottic ones.

In early vocal cord carcinoma, radiation therapy is considered the best treatment with 90 per cent 5-year cure rate. Treatment failures have been analysed by many authors. In the previous report (INOUE et coll. 1969), one of the failures was due to incorrect apprehension of tumor extension, and the other was a well differentiated lesion with poor response to ordinary irradiation.

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Table 1

Age and sex distribution of T1N0 glottic carcinoma (1959–1970)

Age	Male	Female
30–34	1	—
35–39	1	—
40–44	2	—
45–49	8	—
50–54	8	2
55–59	18	2
60–64	15	—
65–69	19	—
70–74	7	—
75–79	7	—
80–84	1	—

This report is based on a retrospective analysis of 91 early carcinomas of the vocal cords, as to the survival and cure rates, survival rates with preserved larynx, recurrences, treatment of recurrences, cause of death, and other primary malignancies.

Material and Methods

From 1959 through 1970, 91 early cases of histologically proven squamous cell carcinomas of the vocal cord (T1N0M0) were treated by radical radiation therapy. The patients were classified according to the TNM system proposed by the UICC (1968). Excluding one patient who was lost after 5 years observation, the other 90 patients could be followed up until the end of 1973. Therefore, all patients were observed for at least 3 years.

The age and sex distribution appears in Table 1. The youngest patient was a male 34 years old, the oldest, a male 80 years old. The ages of the majority of the patients (86 per cent) varied between 50 and 70 years, with a mean age of 62 years for males and 53 years for females.

Four patients were treated with 190 kV using a pendulum irradiation (3 cm × 4 cm, 180° arc) before August 1961; 63 patients were treated with a ^{137}Cs gamma ray unit using parallel opposing fields (size 4 cm × 5 cm or 5 cm × 5 cm, 40 cm SSD) until the end of 1968. Thereafter, 24 patients were treated with ^{60}Co through parallel opposing fields (size 5 cm × 5 cm, 60 cm SSD). In 1966, the fractionation was changed from 6 times per week to 5 times per week. In general, the total tumor dose at a depth of 3 cm was 5 500 rad (22 fractions in 4½ weeks) or 7 000 rad (35 fractions in 7 weeks).

Results

Crude and determinate survival rates appear in Table 2. Some of the patients, who developed local recurrence after primary irradiation, were operated upon and

Table 2

Survival rates of T1 N0 glottic carcinoma treated by radical radiation therapy (1959–1970)

Year	Crude per cent	Determinate per cent
1	99 (90/91)	100 (90/90)
3	89 (81/91)	96 (81/84)
5	86 (59/69)	95 (59/62)
8	75 (33/44)	92 (33/36)
10	76 (16/21)	100 (16/16)

permanent cure was obtained. Thus, it seems unsatisfactory to assess the treatment results of early carcinoma of the vocal cords by survival figures alone. In the present analysis, the cure rate with primary irradiation was evaluated by a slightly modified life table method (Table 3). Of 21 patients who developed local recurrences, 17 recurred within 2 years. It seemed that the subglottic extension was erroneously estimated in the majority of these cases, as previously reported (INOUE et coll.). However, 2 patients recurred at 4 and 9 years, respectively, after completion of radiation therapy. A long term follow-up is thus necessary.

With irradiation only, 70 of 91 patients (77 per cent) were locally cured. Of 21 patients with local recurrence, 12 underwent total laryngectomy, and 8 of them were controlled at the end of 1973. Partial laryngectomy was performed in 3 patients with local recurrence; 1 patient only was cured. This latter case had a highly differentiated squamous cell carcinoma; the other 2 patients subsequently underwent total laryngectomy. Four patients were treated with repeat irradiation without satisfactory result; two were finally operated upon with total laryngectomy (Table 4).

Table 3

Actuarial cure rate of T1N0 glottic carcinoma (1959–1970). DID: Died of intercurrent disease

Year of observ.	No. of cases at risk	Recurrence dur. interval	Lost and DID dur. interval	Withdrawn alive dur. interval	Proportion recurring	Proportion without recurrence	Cumulative recurrence free rate
0–1	91	6	1	—	6.6	93.4	93.4
1–2	84	11	2	—	13.3	86.7	81.0
2–3	71	2	3	—	2.9	97.1	78.7
3–4	66	—	—	10	0	100	78.7
4–5	56	1	1	7	1.9	98.1	77.2
5–6	47	—	2	2	0	100	77.2
6–7	43	—	3	3	0	100	77.2
7–8	37	—	1	9	0	100	77.2
8–9	27	1	—	6	4.2	95.8	73.9
9–10	20	—	—	7	0	100	73.9

Table 4

91 patients with T1N0 glottic carcinoma (1959–1970). NED: No evidence of disease. DT: Death from primary tumor. DID: Death from intercurrent disease. D. other Ca.: Death from other primary carcinoma

	Cured (70)	Recurrences (21)*				
		Total laryng.	Partial laryng.	Partial, later total laryng.	Irradiation	Irradiation, later total laryng.
NED	56	8	1	1		2
DID	8	1				
D. other Ca.	4	1				
DT		2		1	1	1
Lost	1					
Death from traffic accident	1					

* Two refused treatment: 1 died of primary tumour and 1 of suicide.

Four patients developed metastatic cervical lymph nodes after the completion of the primary irradiation. Two of them underwent radical neck dissection with total laryngectomy, and one neck dissection following total laryngectomy. The other one developed lymph node metastases after total laryngectomy and was irradiated. Of the 21 patients with local recurrence, the 5-year survival rate was 68 per cent. Survival rate with preserved larynx appears in Table 5. Eighteen patients underwent total laryngectomy, of these 17 for local recurrence and 1 for other primary carcinoma of the trachea.

The majority of the local recurrences appeared in the anterior commissure and in the subglottic region (Table 6) and behaved as advanced glottic tumors. However, in 2 cases the recurrence extended posteriorly upwards, appearing as an advanced supraglottic tumor.

Table 5

Survival rate with retaining larynx in T1N0 glottic carcinoma (1959–1970)

Year	Crude per cent	Determinate per cent
1	95 (86/91)	96 (86/90)
3	75 (68/91)	81 (68/84)
5	71 (49/69)	79 (49/62)
8	64 (28/44)	78 (28/36)
10	71 (15/21)	94 (15/16)

Table 6

Type of recurrence in T1N0 glottic carcinoma treated by irradiation

Type	No. patients
Localized	2
Anterior commissure	6
Subglottic	10
Supraglottic	2
Unclassified	1

Cause of death and other primary tumors. Of 91 patients treated, 22 had died of various causes by the end of 1973: 6 from recurrent primary lesions, 9 from intercurrent diseases, 1 from suicide, 1 from traffic accident, and 5 from other malignancies (Table 4).

Other primary tumors were found in 8 patients; 2 at the time of the laryngeal carcinoma; the other 6 occurred later. The longest interval between the primary and the second carcinoma was 8 years. Considering the site of the lesion, 2 were found in the stomach, 2 in the colon, 1 in the maxillary sinus, 1 in the floor of mouth, 1 in the oropharynx and 1 in the trachea. One patient with gastric tumor and the 2 with carcinoma of the colon were cured by radical surgery, but one patient died from gastric carcinoma and all the 4 patients with head and neck carcinoma died.

Discussion

T1N0M0 lesions of glottic tumors have a good prognosis. In the survey by VERMUND (1970), there were 751 5-year survivals among 967 patients treated by primary irradiation (78 per cent) as compared with 378 of 458 patients treated by primary surgery (83 per cent). He stated that irradiation was to be preferred in stage I, because of high cure rate with a normal voice practically preserved. MORRISON (1971) reported that the overall 5-year cure rate of 65 per cent was the same among patients treated by laryngofissure and those treated by orthovoltage radiation, but the functional results after radiation therapy were better than after surgery. However, HARRIS (1961) suggested that partial laryngectomy should be performed for well differentiated lesions.

In the present report 2 kinds of survival rates appear, as VERMUND (1970) emphasized the importance of a comparison between the crude and the determinate survival data, because there was a considerable death rate from intercurrent diseases.

If a recurrence develops, this occurs within 2 years in the majority of cases, as reported by many authors; in a few cases late recurrences may be encountered, however. Also in this material, two late recurrences appeared. Thus, a long term follow-up is necessary for these patients. The majority of recurrences extended to the anterior commissure or to the subglottic regions. MÅRTENSSON et coll. (1967) reported

that the primary examination of the tumor had been unsatisfactory in the cases of subglottic extension. He also reported that total laryngectomy was to be preferred for recurrent cases, primarily irradiated, resulting in a 5-year survival of 69 per cent in his series. Also in the present material, total laryngectomy in cases with radiation failure resulted in 68 per cent survival at 5 years. Partial laryngectomy has also been suggested in cases with small recurrences and good results have been obtained. However, in old patients, partial laryngectomy for recurrent lesion involves much more difficulties than total laryngectomy. As with glottic carcinoma, patients are often very old; total laryngectomy is thus to be preferred in recurrences after radiation therapy. A repeat irradiation of a recurrence following primary radiation therapy is hazardous and rarely indicated (VERMUND 1970). In the present material, 4 patients were treated with re-irradiation without success, 2 were finally cured by total laryngectomy, 2 refused laryngectomy and died from advanced local disease.

Six patients died from laryngeal carcinoma, but none from distant metastases or lymph node metastases in the neck. Other primary malignant tumors developed in 9 per cent of the cases. SATO et coll. (1971) reported that 35 out of 692 patients with laryngeal carcinoma developed other primary tumors until the end of 1970 at our hospital. The incidence of other primary malignancies is thus very high among patients with early carcinoma of the vocal cords. In the material of Tl glottic carcinoma reported by GOFFINET et coll. (1973), 10 of 78 patients developed other primary tumors. It seems likely that the advanced age of the patients and the high curability of the glottic carcinoma resulted in this high incidence of other primary malignancies.

SUMMARY

A material of 91 early carcinomas of the vocal cord treated by radiation therapy were reviewed. The 5-year crude and determinate survival rates were 86 and 95 per cent, respectively. Primary irradiation only, resulted in a 5-year cure rate of 77 per cent. Of the 21 patients who developed local recurrences, 11 were cured by total, and one by partial laryngectomy. Eight patients developed other primary carcinomas.

ZUSAMMENFASSUNG

Die Verfasser behandeln zusammanfassend ein Material von 91 frühen Karzinomen des Stimmbands, die mit Bestrahlung behandelt worden waren. Die grobe und die schliessliche 5-Jahres Überlebensraten betrugen 86 bzw. 95%. Eine ausschliessliche primäre Bestrahlung führte zu einer groben 5-Jahres Heilungsrate von 77%. Von den 21 Patienten, bei denen sich lokale Rezidive entwickelt hatten, wurden 11 durch totale und einer durch partielle Laryngektomie geheilt. Acht Patienten entwickelten andere primäre Karzinome.

RÉSUMÉ

Les auteurs ont passé en revue une série de 91 carcinomes de la corde vocale au début traités par les radiations. Les taux brut et définitif de survie à 5 ans ont été respectivement

de 86 et 95%. L'irradiation primaire isolée donne un taux de survie à 5 ans de 77%. Parmi les 21 malades qui ont présenté des récidives locales, 11 ont été soignés par laryngectomie totale et 1 par laryngectomie partielle. Huit malades ont présenté d'autres carcinomes primitifs.

REFERENCES

DUNHAM L. J. and BAILOR III J. C.: World maps of cancer mortality rate and frequency ratios. J. nat. Cancer Inst. 41 (1968), 155.

GOFFINET D. R., ELTRINGHAM J. R., GLATSTEIN E. and BAGSHAW M. A.: Carcinoma of the larynx. Results of radiation therapy in 213 patients. Amer. J. Roentgenol. 117 (1973), 553.

HARRIS H. H.: Deficits in irradiation therapy for carcinoma of the larynx followed by surgery. Ann. Otol. (St. Louis) 70 (1961), 463.

INOUE T., KANEMITSU M. and SHIGEMATSU Y.: Radiotherapy of laryngeal carcinoma with special reference to the treatment policy of cordal cancer. Nippon Acta radiol. 29 (1969), 322.

IWAMOTO H.: Cancer of the larynx in Japan. Laryngoscope 81 (1971), 387.

MÅRTENSSON B., FLUUR E. and JACOBSSON F.: Aspects on treatment of cancer of the larynx. Ann. Otol. (St. Louis) 76 (1967), 313.

MORRISON R.: Review article. Radiation therapy in diseases of the larynx. Brit. J. Radiol. 44 (1971), 489.

SATO T., SAKAI S. and IKEDA H.: Multiple primary cancers in patients of laryngeal, hypopharyngeal and maxillary cancers. Otologica Fukuoka 17 (1971), 51.

SEGI M., KURIHARA M. and MATSUYAMA T.: Cancer mortality in Japan (1899–1962). Dept. of Public Health. Tohoku University School of Medicine, Sendai, Japan, 1965.

SMITH R. R., CAULK R., FRAZELL E., HOLINGER P. H., MACCOMB W. S., RUSSELL W. D., SCHULZ M. D. and TUCKER G. F.: Revision of the clinical staging system for cancer of the larynx. Cancer 31 (1973), 72.

VERMUND H.: Role of radiotherapy in cancer of the larynx as related to the TNM system of staging. A review. Cancer 25 (1970), 485.